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#31	Search **"transgenic mice" and "human and antibody" and expression**	10:30:08	802
#30	Search **"transgenic mice" and "human and antibody"**	10:29:59	1753
#29	Search **"transgenic mice" and human and antibody**	10:29:42	1753
#28	Search **"transgenic mice"**	10:29:22	37386
#27	Search **human antibody expression and "transgenic mice"**	10:29:05	802
#25	Search **Bruggemann m**	10:27:43	72
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#23	Search **"human monoclonal antibody" and mice**	10:23:07	232
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#20	Search **"monoclonal" and transgenic**	09:51:38	1569
#19	Search **"monoclonal Ab" and transgenic**	09:51:21	3
#18	Search **"monoclonal Ab" and transgene**	09:51:16	0
#17	Search **"monoclonal Ab" and transgene mice**	09:51:09	0
#13	Search **"monoclonal Ab" and "transgenic mice"**	09:48:35	3
#10	Search **"immunoglobulin and "transgenic mice"**	09:46:14	27
#9	Search **"immunoglobulin and transgenic mice"**	09:42:46	6377
#8	Search **immunoglobulin transgenic mice**	09:42:25	6377
#7	Search **human and immunoglobulin "transgenic mice" and**	09:41:29	1418
#5	Search **"human immunoglobulin" "transgenic mice" and Th1**	09:37:56	1
#4	Search **"human immunoglobulin" "transgenic mice" and Th2**	09:37:39	0
#3	Search **"human immunoglobulin" "transgenic mice"**	09:34:57	67

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Set	Items	Description
S1	0	TRANSGENIC W MOUSE OR TRANSGENIC W MICE
S2	0	TRANSGENIC W MOUSE
S3	0	TRANSGENIC W MOUSE
S4	2093342	MOUSE
S5	313583	TRANSGEN?
S6	117	XENOMOUSE
S7	1	HUMAB-MOUSE
S8	7016	HUMAN (N) MONOCLONAL (N) ANTIBODY
S9	37596	TH1 AND TH2
S10	129888	S4 AND S5
S11	46	S10 AND S6
S12	9	S11 AND S8
S13	57	S10 AND S8
S14	0	S13 AND S9
S15	387089	MONOCLONAL (N) ANTIBODY
S16	2931	S10 AND S15
S17	79	S16 AND S9
S18	45	IL (W) 4 AND S17
S19	41	INTERLEUKIN (W) 4 AND S17
S20	37	RD S19 (unique items)
S21	38	RD S18 (unique items)
S22	0	C57BL/6 (N) ANTIBODY (N) PRODUCTION
S23	1066	C57BL/6
S24	42298	DS
S25	56427	ANTIBOD? (N) PRODUCTION
S26	7	S23 AND S25
S27	7	RD (unique items)
S28	35	S23 AND S15
S29	35	RD S28 (unique items)
S30	0	S9 AND "ANTIBOD? (N) SYNTHESIS
S31	5128	ANTIBODY (N) SYNTHESIS
S32	45	S31 AND S9
S33	25	RD (unique items)

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                  to core patent offices
 NEWS  6  OCT 13  New CAS Information Use Policies Effective October 17, 2005
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 NEWS 10  OCT 27  EPFULL enhanced with additional content
 NEWS 11  NOV 14  CA/CAplus - Expanded coverage of German academic research
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                  spectral property data
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=> s transgen? (N) mouse
         81150 TRANSGEN?
        778180 MOUSE
L1       12904 TRANSGEN? (A) MOUSE

=> s Th1 (p) Th2
         14830 TH1
         13605 TH2
L2        9034 TH1 (P) TH2

=> s monoclonal (w) antibod?
        173749 MONOCLONAL
        586543 ANTIBOD?
L3      152345 MONOCLONAL (W) ANTIBOD?

=> s antibod? (p) synthesis
        586543 ANTIBOD?
        549731 SYNTHESIS
L4       20783 ANTIBOD? (P) SYNTHESIS

=> s L1 and L2 and L3
L5           1 L1 AND L2 AND L3

=> d TI AB

L5   ANSWER 1 OF 1  BIOSIS  COPYRIGHT (c) 2005 The Thomson Corporation  on STN
TI   Interaction within clusters of dendritic cells and helper T cells during
     initial Th1/Th2 commitment.
AB   Cytokines are the main agents known to regulate Th1/Th2
     commitment, where they may operate through paracrine activity within
```

clusters of T cells gathered around dendritic cells (DC). An in vitro system is used here to test this possibility, using clusters around DC composed of naive TCR-transgenic ovalbumin peptide 323-339-specific CD4+ T cells as targets plus TCR-transgenic pigeon cytochrome C peptide 88-104-specific CD4+ polarized **Th1** or **Th2** cells as inducers. The polarized inducer cells exerted their maximum effect when the two T cell populations were activated within the same cluster, implemented by allowing a single DC to present both their epitopes. This finding thus supports the paracrine hypothesis. The system was then employed to explore the role of individual cytokines by means of inhibition by **monoclonal antibodies**. Development of **Th2** commitment proved strictly dependent on the IL-4 produced by the **Th2** inducers. For **Th1** commitment, IFN-gamma and IL-12 were both needed, but with IFN-gamma required only during the initial period of culture. The rapid timing observed under these conditions places constraints on the molecular basis of commitment, and appears accurately to reflect the physiological response in vivo.

```
=> s L1 and L3
L6          188 L1 AND L3

=> s L6 and L4
L7            6 L6 AND L4

=> d TI AB
```

L7 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

TI SV40-derived ribozyme construct mediates effective destruction of human alpha1-antitrypsin transcripts in a **transgenic mouse** model.

AB Background: Human alpha1-antitrypsin (alpha1-AT) deficiency is a genetic disorder that leads to emphysema and chronic liver disease. The lung disease is thought to reflect insufficient normal alpha1-AT activity in the circulation, whereas the liver disease occurs because abnormal alpha1-AT accumulates in hepatocytes. The bi-functional liver-directed approach we are using involves inhibiting abnormal alpha1-AT protein production employing a gene-specific ribozyme, and the **synthesis** of a ribozyme-resistant wild-type protein by engineering a modified alpha1-AT cDNA. Our previous findings showed that the modified human alpha1-AT cDNA delivered by the SV40 vector led to acceptable levels of the human protein in mice for one year. In the present study, we evaluated the efficacy of ribozyme-mediated destruction of targeted human PiZ transcripts in vivo. Methods: Transgenic mice carrying the human alpha1-AT PiZ allele were infected via an indwelling catheter in the portal vein with recombinant SV40 virus containing a ribozyme designed to target human alpha1-AT mRNA. The destruction of PiZ transcripts in ribozyme-treated transgenic mice was evaluated by real time quantitative RT-PCR, and human alpha1-AT in mouse serum was quantified by ELISA, using a specific **monoclonal antibody** against human alpha1-AT. Results: Quantitative RT-PCR analysis revealed that the average reduction of human PiZ transcripts in the mouse livers was 57.1+-18.3% (p=0.05) in four mice that were sacrificed between 6 to 16 weeks after transduction with the ribozyme construct. No change in mouse albumin mRNA was found. The administration of the ribozyme lowered serum levels of human alpha1-AT to 42.4+-12.1% of pretreatment values (p<0.01) 3-25 weeks post-transduction in six mice, whereas serum human alpha1-AT levels in transgenic mice not treated with the ribozyme were unchanged. Serum human alpha1-AT in one mouse was reduced by 99% at 6 weeks, and human alpha1-AT PiZ transcripts were undetectable by quantitative RT-PCR from the liver of that mouse. Moreover, quantitative RT-PCR showed that the levels of mouse alpha1-AT, albumin, and beta-actin mRNA from that mouse remained the same as in control mice despite the essentially complete loss of the human alpha1-AT transcripts. Conclusion: Findings in

the present study demonstrated that an SV40-derived construct containing a ribozyme is highly effective in lowering human alpha1-AT mRNA and protein levels in vivo. When considered together, the results of the present study and our previous reports suggest that our recombinant SV40 virus system represents the first step in the development of a clinically valuable gene therapy approach for alpha1-AT deficiency.

=> d L7 TI 1-6

L7 ANSWER 1 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI SV40-derived ribozyme construct mediates effective destruction of human alpha1-antitrypsin transcripts in a **transgenic mouse** model.

L7 ANSWER 2 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Cellular interactions with a cryptic element within collagen type-I promotes B16 melanoma tumor growth in vitro and in vivo.

L7 ANSWER 3 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Human antibodies by design.

L7 ANSWER 4 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Anti-idiotype **monoclonal antibodies** specific for the MOPC167 anti-phosphocholine transgene-encoded antibody.

L7 ANSWER 5 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI Fetal hemoglobin induction by acetate, a product of butyrate catabolism.

L7 ANSWER 6 OF 6 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN
TI TISSUE-SPECIFIC EXPRESSION OF THE HUMAN RENIN GENE IN TRANSGENIC MICE.

=> File Medline embase caplus scisearch

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L8 1305 L1 AND L3

=> s L8 and L2
L9 27 L8 AND L2

=> duplicate remove
ENTER L# LIST OR (END):L9
DUPLICATE PREFERENCE IS 'EMBASE, CAPLUS, SCISEARCH'
KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):y
ENTER FILE NAMES OF DUPLICATES TO KEEP:n
'N' IS NOT VALID. VALID FILE NAMES ARE 'EMBASE, CAPLUS, SCISEARCH'
You have entered a file name of duplicates to keep that is not

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referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.
ENTER FILE NAMES OF DUPLICATES TO KEEP:
ENTER FILE NAMES OF DUPLICATES TO KEEP:
ENTER FILE NAMES OF DUPLICATES TO KEEP:L9
'L17' IS NOT VALID.  VALID FILE NAMES ARE 'EMBASE, CAPLUS, SCISEARCH'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.
ENTER FILE NAMES OF DUPLICATES TO KEEP:s L(
'S' IS NOT VALID.  VALID FILE NAMES ARE 'EMBASE, CAPLUS, SCISEARCH'
You have entered a file name of duplicates to keep that is not
referenced by any of the L#s specified for this DUPLICATE command.
The file names of duplicates that can be kept are listed above.
Please enter one of these file names.
ENTER FILE NAMES OF DUPLICATES TO KEEP:log Y
'LOG' IS NOT VALID.  VALID FILE NAMES ARE 'EMBASE, CAPLUS, SCISEARCH'
You have entered a file name of duplicates to keep that is not
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Term: L8 and "antibody synthesis"

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Set Name side by side	Query	Hit Count	Set Name result set
DB=PGPB,USPT,USOC,EPAB,JPAB,DWPI; PLUR=YES; OP=ADJ			
L12	L11 and "anti IL-12 antibody"	0	L12
L11	L8 and IL-4	775	L11
L10	L8 and "antibody synthesis"	14	L10
L9	L8 and "antibody adj synthesis"	0	L9
L8	L7 and "antibody production"	867	L8
L7	L6 and Th1	1310	L7
L6	L3 and Th2	1416	L6
L5	L3 and Th2	1416	L5
L4	"monoclonal adj antibody"	0	L4
L3	L1 and "monoclonal antibody"	12568	L3
L2	L1 and "human and antibody and expression"	0	L2
L1	"transgenic mouse"	17819	L1

END OF SEARCH HISTORY